

THE RELATIVE PROPORTIONS OF STEREOISOMERIC  
OXIMES FORMED IN THE OXIMATION OF  
UNSYMMETRICAL KETONES

---

A DISSERTATION  
SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS  
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN THE  
UNIVERSITY OF MICHIGAN

---

BY  
SISTER M. XAVERIA BARTON, I. H. M.

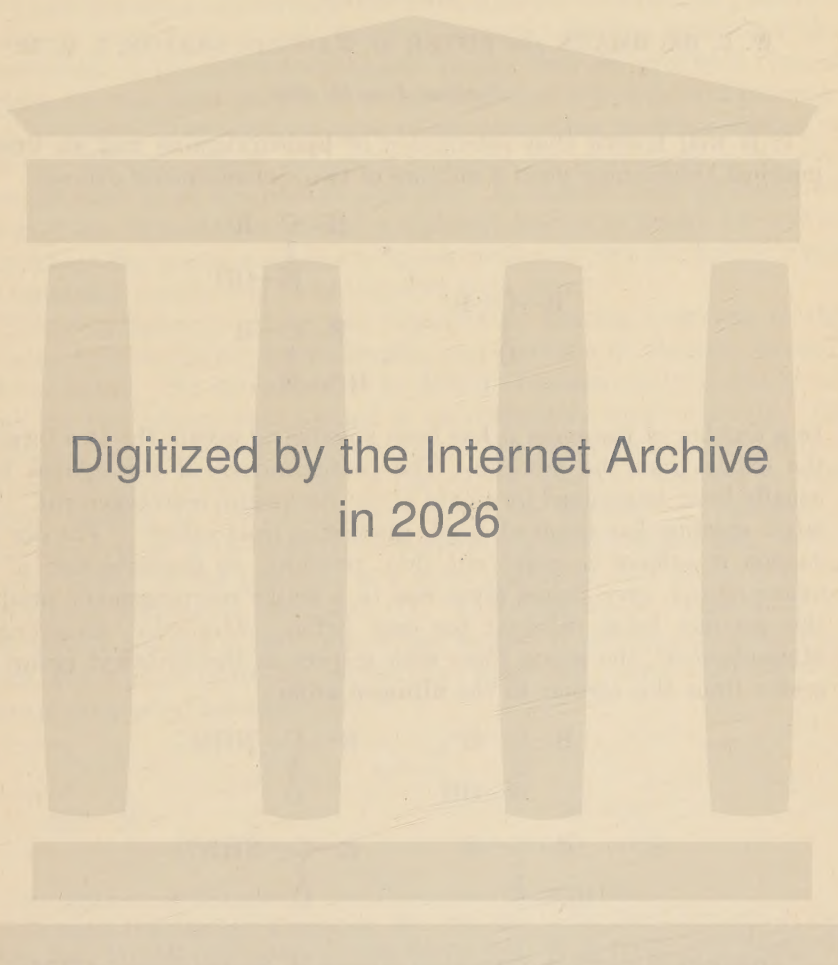
---

1938

Reprinted from THE JOURNAL OF ORGANIC CHEMISTRY  
Vol. 3, No. 4, September, 1938







Digitized by the Internet Archive  
in 2026

[https://archive.org/details/IA41549008\\_0045](https://archive.org/details/IA41549008_0045)



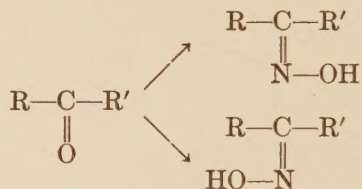
[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

## THE RELATIVE PROPORTIONS OF STEREOISOMERIC OXIMES FORMED IN THE OXIMATION OF UNSYMMETRICAL KETONES

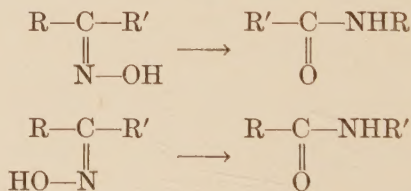
W. E. BACHMANN AND SISTER M. XAVERIA BARTON, I. H. M.\*

Received June 28, 1938

It is well known that interaction of hydroxylamine and an unsymmetrical ketone may yield a mixture of two stereoisomeric oximes.



In a number of instances it has been possible to isolate the two forms of the oxime from the mixture. The configurations of the oximes have usually been determined by means of the Beckmann rearrangement. The latter reaction has received ample discussion from others<sup>1</sup>. For our discussion it suffices to point out that, provided no isomerization of the oxime occurs, each oxime gives rise to a single rearrangement product, this product being different for each oxime. Moreover, according to Meisenheimer<sup>2</sup>, the group *trans* with respect to the hydroxyl group migrates from the carbon to the nitrogen atom.



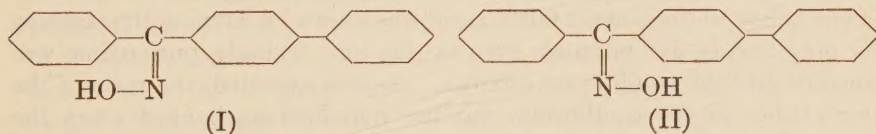
\* From part of the Ph.D. dissertation of Sister M. Xavieria Barton, I.H.M.

<sup>1</sup> Excellent reviews of the Beckmann rearrangement have been presented by BLATT, *Chem. Rev.* **12**, 215-260 (1933), and by MEISENHEIMER AND THEILACKER in FREUDENBERG, "Stereochemie," Franz Deuticke, Leipzig, **1933**, Part III, pp. 1002-1094. See also GILMAN, "Organic Chemistry," John Wiley and Sons, New York, **1938**, Vol. I.

<sup>2</sup> MEISENHEIMER, *Ber.*, **54**, 3206 (1921).

Although a large amount of work has been done on the Beckmann rearrangement itself, little attention has been directed to the quantitative estimation of the relative amounts of the two stereoisomeric oximes that are formed under a given set of conditions. Recently, Bachmann and Boatner<sup>3</sup> investigated the oximation of the structurally isomeric acetylphenanthrenes and benzoylphenanthrenes and determined the relative amounts of the two oximes that were produced in each case. We have now extended this investigation to include the oximation of a number of simple diaryl ketones and alkyl aryl ketones. Having determined the proportions of the two stereoisomeric oximes that are produced from a ketone, we were next interested in knowing what this ratio really means. Is it a measure of the relative rates of two competing reactions leading to the two different oximes, or does it represent the proportions of the two stereoisomers in an equilibrium mixture? To answer these questions we studied the oximation of phenyl *p*-biphenyl ketone in detail, for it was found that the two stereoisomeric oximes produced from this ketone could be separated readily and be obtained in pure form.

Phenyl *p*-biphenyl ketone was oximated by heating a mixture of the ketone, hydroxylamine hydrochloride, and pyridine in absolute alcohol<sup>4</sup> for two hours. By the method to be described subsequently, it was found that the two oximes were formed in approximately equal amounts. By fractional crystallization we next isolated the two stereoisomeric oximes in pure, crystalline form<sup>5</sup>. One of the oximes, which crystallized in large prisms melting at 173°, rearranged under the influence of phosphorus pentachloride to *N*-(*p*-biphenyl)benzamide,  $\text{C}_6\text{H}_5\text{CONHC}_6\text{H}_4\text{C}_6\text{H}_5$ , exclusively; hence, on the principle of a *trans* migration, this oxime must be *syn*-phenyl *p*-biphenyl ketoxime† (I). The other oxime, crystallizing in fine needles melting at 200°, rearranged to give *N*-phenyl-*p*-phenylbenzamide,  $\text{C}_6\text{H}_5\text{C}_6\text{H}_4\text{CONHC}_6\text{H}_5$ , exclusively; hence this oxime must be *anti*-phenyl *p*-biphenyl ketoxime (II).



<sup>3</sup> BACHMANN AND BOATNER, *J. Am. Chem. Soc.*, **58**, 2097 (1936).

<sup>4</sup> Compare HOUBEN AND PFANKUCH, *Ber.*, **59**, 2394 (1926), BUCK AND IDE, *J. Am. Chem. Soc.*, **53**, 1541 (1931), BRYANT AND SMITH, *ibid.*, **57**, 57 (1935), and BACHMANN AND BOATNER, *ibid.*, **58**, 2097 (1936), for the pyridine method of preparing oximes.

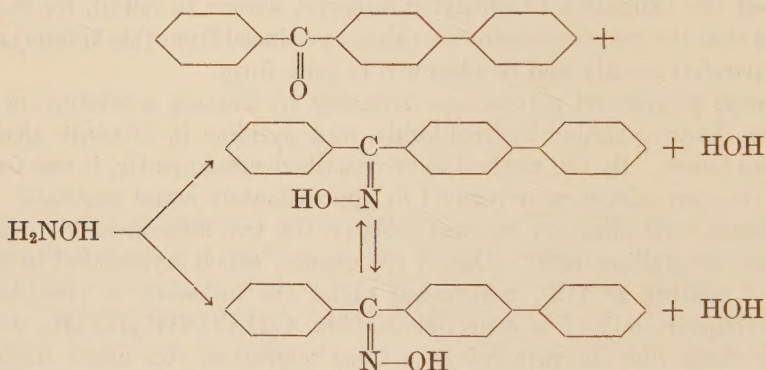
<sup>5</sup> KOLLER, *Monatsh.*, **12**, 501 (1891), was able to isolate only one of the oximes, although, as will be shown in the experimental part, the product prepared according to his procedure actually contained both oximes.

† The prefix, *syn* or *anti*, refers to the position of the first group named relative to the hydroxyl group. This oxime (I) could also be called *anti*-*p*-biphenyl phenyl ketoxime.



The fact that only one rearrangement product was obtained in each case is of importance in demonstrating that pure oximes had been isolated, and, secondly, that no isomerization of one stereoisomer to the other occurred under the conditions employed for the rearrangement.

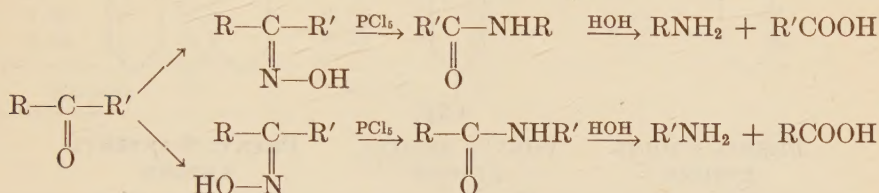
Each of the pure oximes was now heated with a mixture of hydroxylamine hydrochloride, pyridine, absolute alcohol and a few drops of water for two hours. Under these conditions, which simulated those used for the oxidation of the ketone, each of the oximes was converted to a 1:1 mixture of the *syn* and *anti* forms, the identical mixture that was obtained when the ketone was oximated. This means that each oxime is convertible to its geometrical isomer under the conditions employed for oximation, and it follows that the 1:1 mixture represents an *equilibrium* mixture of the *syn* and *anti* forms. The oximation of the ketone can, therefore, be formulated as follows,



Although the rate of formation of one oxime may be greater than that of the other, this factor will have no effect on the final proportions if sufficient time is allowed for equilibrium to be established. That the conversion of one oxime to the other is fairly rapid was shown by running the reaction for only twenty-five minutes; even in this time a single, pure oxime was converted to the equilibrium mixture. As was expected, the ratio of the two oximes in the equilibrium mixture remained unchanged when the oximation mixture was heated for two days.

It should be borne in mind that the scheme shown above represents the over-all state of affairs and does not attempt to account for the mechanism by which the change from one oxime to the other takes place. There may be an equilibrium between the oximes themselves, or through intermediate oxime salts, or the mechanism might involve hydrolysis of the oxime through a reversible reaction with re-oximation of the regenerated ketone. These points as well as the speed of the interconversion and the reagent catalyzing the change await solution from further experiments.

In order to determine the relative amounts of the two stereoisomeric oximes produced from a given ketone, we employed the procedure of Bachmann and Boatner<sup>3</sup>. The crude mixture of oximes was subjected to rearrangement, without any purification of the oximes by recrystallization, for it would be impossible to avoid some loss if this were done. Other investigators have been content to recrystallize the mixture of oximes and isolate the isomer present in the larger amount. Following the rearrangement, we hydrolyzed the mixture of substituted amides, and the relative proportion of the two different acids (or amines) which were produced was taken as a measure of the amounts of the original oximes in the mixture. The complete scheme may be represented as follows,



The relative amount of the acid RCOOH represents the relative proportion of the oxime having the group R *syn* to the hydroxyl group.

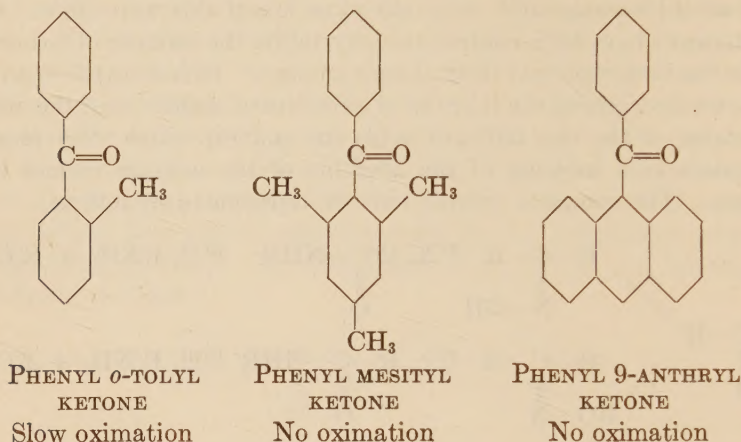
In general, oximation was accomplished by the method already mentioned, namely, heating the ketone with hydroxylamine hydrochloride and pyridine in absolute alcohol for two hours. With all of the ketones listed in Table II, except 2-benzoylfluorene, the oximes remained in solution. By this method we were able to obtain quantitative oximation of all of the ketones which we studied with the exception of the 9-anthryl ketones. The failure in these cases is attributed to steric hindrance around the carbonyl group. Steric hindrance had already been encountered in the *o*-tolyl aryl ketones, for longer periods of time were required in order to oximate them completely. Smith<sup>6</sup> endeavored to prepare the oxime of mesityl phenyl ketone but even the most drastic conditions failed to yield the oxime. A comparison of the structures of 9-anthryl phenyl ketone with the *o*-methyl substituted ketones shows why the negative results obtained with the 9-anthryl ketones were not entirely unexpected, for two ortho groups are present to hinder the formation of the oxime.

The second requirement for our investigation was quantitative rearrangement of the ketoximes. Phosphorus pentachloride in anhydrous benzene was selected as the best reagent for carrying out the Beckmann rearrangement, because in all cases it was possible to obtain at room temperature a quantitative yield of the substituted amide in a relatively pure condition. Phosphorus trichloride and sulfuric acid-acetic acid were

<sup>6</sup> SMITH, *Ber.*, **24**, 4025 (1891).



found to be less satisfactory for our purpose. Although we obtained only partial rearrangement with phosphorus trichloride, the latter can now be added to the list of reagents capable of inducing the Beckmann rearrangement. Other reagents were less desirable because they frequently re-



quired heating or were incomplete in their reaction. It has been reported that certain oximes, particularly the aliphatic ketoximes, isomerize to some extent during the process of rearrangement, especially under the influence of heat. We feel that under our conditions, there is practically no conversion of one form of the oxime to the other—and this was definitely shown to be true with the phenyl *p*-biphenyl ketoximes.

The mixtures of substituted amides produced on rearrangement of the oximes were generally resistant to hydrolysis. Best results were obtained by refluxing the mixture with a methanol solution of potassium hydroxide for four days or longer. The removal of the acids from the hydrolysis mixture and the analysis of the mixture of acids varied with the particular mixture involved. In Table I is given a typical set of data obtained with one ketone, *p*-biphenyl *m*-tolyl ketone, which shows the agreement obtained on different runs. The yield of acids is calculated on the basis of the ketone. The proportion of *p*-phenylbenzoic acid represents the relative amount of the *syn-p*-biphenyl *m*-tolyl ketoxime (53 per cent.) and the quantity of *m*-toluic acid corresponds to the proportion of *anti-p*-biphenyl *m*-tolyl ketoxime (47 per cent.) in the mixture of the *syn* and *anti* oximes.

In Table II are summarized the results obtained with thirteen ketones, of which all but one (*o*-tolyl *p*-biphenyl ketone) gave yields of acids corresponding to 88–98 per cent. of the theoretical amount. Not listed are the ketones which failed to give satisfactory results in some stage of the



process; mention of these is made in the experimental part. The figures representing the proportions of *syn* and *anti* oximes in the mixtures obtained on oximation are accurate only to 5-10 per cent. In nearly all cases two hours of heating was employed for the oximation, so that the

TABLE I

PROPORTIONS OF ACIDS PRODUCED BY HYDROLYSIS OF THE AMIDES FORMED BY REARRANGEMENT OF THE OXIMES OF *p*-BIPHENYL *m*-TOLYL KETONE

| <i>p</i> -PHENYLBENZOIC ACID |            | <i>m</i> -TOLUIC ACID |            | TOTAL ACID |            |
|------------------------------|------------|-----------------------|------------|------------|------------|
| g.                           | % by moles | g.                    | % by moles | g.         | % by moles |
| 2.01                         | 53.5       | 1.20                  | 46.5       | 3.21       | 95         |
| 1.00                         | 55.6       | 0.55                  | 44.5       | 1.55       | 91         |
| 0.99                         | 51.5       | 0.65                  | 48.7       | 1.64       | 98         |
| Average                      | 53         | Average               | 47         |            |            |

TABLE II

PROPORTIONS OF *Syn* AND *Anti* OXIMES IN THE MIXTURES PRODUCED BY OXIMATION OF THE KETONES

| KETONE<br>R-C(=O)-R' |                        | %<br>R-C(=O)-R'<br>HO-N | %<br>R-C(=O)-R'<br>N-OH |
|----------------------|------------------------|-------------------------|-------------------------|
| R                    | R'                     |                         |                         |
| Phenyl               | <i>p</i> -Biphenyl     | 49                      | 51                      |
| Phenyl               | <i>p</i> -Tolyl        | 48                      | 52                      |
| Phenyl               | <i>m</i> -Tolyl        | 50                      | 50                      |
| Phenyl               | <i>o</i> -Tolyl        | 23                      | 77                      |
| Phenyl               | <i>p</i> -Anisyl       | 51                      | 49                      |
| Phenyl               | <i>p</i> -Chlorophenyl | 44                      | 56                      |
| Phenyl               | 2-Fluoryl              | 46                      | 54                      |
| <i>o</i> -Tolyl      | <i>p</i> -Biphenyl     | 66                      | 34 <sup>a</sup>         |
| <i>m</i> -Tolyl      | <i>p</i> -Biphenyl     | 47                      | 53                      |
| <i>p</i> -Tolyl      | <i>p</i> -Biphenyl     | 34                      | 66                      |
| Methyl               | 1-Naphthyl             | 99                      | 1                       |
| Methyl               | 2-Naphthyl             | 99                      | 1                       |
| Methyl               | <i>p</i> -Biphenyl     | 99                      | 1                       |

<sup>a</sup> These values are based on a 75% yield of acids.

results indicate the proportions of the two forms of the oxime in the mixture at the end of this time. Whether or not an equilibrium mixture was obtained in each case cannot be stated with certainty. This can be ascertained by isolating the two oximes as was done for the phenyl *p*-biphenyl ketoximes and determining whether conversion of one form to the other

takes place under the conditions of the oximation. Once the interconversion of the oximes has been established for all cases, the position of equilibrium could be determined by running the oximation reaction for varying periods of time.

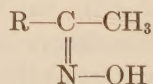
From the table it is seen that most of the diaryl ketones yielded the *syn* and *anti* oximes in an approximately 1:1 ratio. The methyl aryl ketones gave nearly entirely the *syn*-methyl form, although about 1 per cent. of the other form was present in the mixture. This result is in agreement

TABLE III  
NEW SUBSTITUTED AMIDES  
(All of the compounds are colorless.)

| AMIDE                                                                         | RECRYST.<br>SOLVENT | CRYST. FORM | M.P., °C. |
|-------------------------------------------------------------------------------|---------------------|-------------|-----------|
| <i>N</i> -Methyl- <i>p</i> -phenylbenzamide <sup>a</sup> .....                | Alcohol             | Needles     | 167       |
| <i>N</i> -( <i>o</i> -Tolyl)- <i>p</i> -phenylbenzamide <sup>b</sup> .....    | Benzene             | Needles     | 179.5-180 |
| <i>N</i> -( <i>p</i> -Biphenyl)- <i>o</i> -methylbenzamide <sup>c</sup> ..... | Benzene             | Needles     | 256       |
| <i>N</i> -( <i>m</i> -Tolyl)- <i>p</i> -phenylbenzamide <sup>d</sup> .....    | Acetone             | Plates      | 165-166   |
| <i>N</i> -( <i>p</i> -Biphenyl)- <i>m</i> -methylbenzamide <sup>e</sup> ..... | Acetone             | Flakes      | 270       |
| <i>N</i> -( <i>p</i> -Tolyl)- <i>p</i> -phenylbenzamide <sup>f</sup> .....    | Acetone             | Flakes      | 230-231   |
| <i>N</i> -( <i>p</i> -Biphenyl)- <i>p</i> -methylbenzamide <sup>g</sup> ..... | Alcohol             | Plates      | 236-237   |
| <i>N</i> -Methyl-1-naphthamide <sup>h</sup> .....                             | Benzene             | Needles     | 159-160   |
| <i>N</i> -Methyl-2-naphthamide <sup>i</sup> .....                             | Benzene             | Plates      | 108-109.5 |
| <i>N</i> -Phenyl- <i>m</i> -methylbenzamide <sup>j</sup> .....                | Benzene             | Rhombs      | 125-125.5 |
| <i>N</i> -(2-Fluoryl)benzamide <sup>k</sup> .....                             | Benzene             | Flakes      | 215       |
| <i>N</i> -Phenyl-2-fluorene-carboxylic acid amide <sup>l</sup> ...            | Acetone             | Flakes      | 255-256   |

<sup>a</sup> Calc'd for C<sub>14</sub>H<sub>13</sub>NO: N, 6.3. Found: N, 6.3. <sup>b</sup> Calc'd for C<sub>20</sub>H<sub>17</sub>NO: N, 4.9. Found: N, 4.9. <sup>c</sup> Calc'd for C<sub>20</sub>H<sub>17</sub>NO: N, 4.9. Found: N, 4.8. <sup>d</sup> Calc'd for C<sub>20</sub>H<sub>17</sub>NO: N, 4.9. Found: N, 4.6. <sup>e</sup> Calc'd for C<sub>20</sub>H<sub>17</sub>NO: N, 4.9. Found: N, 4.8. <sup>f</sup> Calc'd for C<sub>20</sub>H<sub>17</sub>NO: N, 4.9. Found: N, 4.7. <sup>g</sup> Calc'd for C<sub>20</sub>H<sub>17</sub>NO: N, 4.9. Found: N, 4.6. <sup>h</sup> Calc'd for C<sub>12</sub>H<sub>11</sub>NO: N, 7.6. Found: N, 7.4. <sup>i</sup> Calc'd for C<sub>12</sub>H<sub>11</sub>NO: N, 7.6. Found: N, 7.5. <sup>j</sup> Calc'd for C<sub>14</sub>H<sub>13</sub>NO: N, 6.6. Found: N, 6.5. <sup>k</sup> Calc'd for C<sub>20</sub>H<sub>15</sub>NO: N, 4.9. Found: N, 4.9. <sup>l</sup> Calc'd for C<sub>20</sub>H<sub>15</sub>NO: N, 4.9. Found: N, 4.9.

with the results obtained by Bachmann and Boatner with the acetyl-phenanthrenes. They found that the 1-, 2-, 3-, and 9-phenanthryl groups oriented themselves nearly entirely *anti* to the hydroxyl group. In all of these methyl aryl ketones, then, the configuration of the oxime is principally



No ketone which we could successfully oximate failed to give two stereoisomers. This is particularly noteworthy in the case of the methyl aryl



ketones, for only one oxime has been reported before for these ketones. It is probable that two oximes are always formed from a given ketone, but the one present in small amount has escaped detection by the ordinary methods of separation. By our procedure we have demonstrated the existence of the following new oximes: *syn-p*-biphenyl methyl ketoxime, *syn*-phenyl *p*-biphenyl ketoxime, *syn-o*-tolyl *p*-biphenyl ketoxime, *anti-o*-tolyl *p*-biphenyl ketoxime, *syn-m*-tolyl *p*-biphenyl ketoxime, *anti-m*-tolyl *p*-biphenyl ketoxime, *syn-* or *anti-p*-tolyl *p*-biphenyl ketoxime\*, *syn-* or *anti-m*-tolyl phenyl ketoxime\*, *syn-* or *anti-* phenyl 2-fluoryl ketoxime\*, *syn*-1-naphthyl methyl ketoxime, *syn*-2-naphthyl methyl ketoxime, *syn*-methyl 1-anthryl ketoxime, *anti*-methyl 1-anthryl ketoxime. For the oximes marked with an asterisk, one form of the oxime has already been reported in the literature but the configuration has not been established; our work shows that both forms of these oximes exist.

A number of the substituted amides, which were obtained as products of the rearrangement of the oximes, have not been prepared before. These new amides have now been synthesized in quantitative yield by mixing equimolar quantities of the acid chloride and the amine in benzene or acetone solution. The properties of these new amides are shown in Table III.

#### EXPERIMENTAL

*Oximation of the ketones.*—In all cases a mixture was made of 0.01 gram mole of the ketone and 0.011 gram mole of hydroxylamine hydrochloride in enough pyridine and absolute alcohol (usually 4 to 5 cc. of each) to dissolve all of the reactants when warm. After the mixture had been heated on a steam bath for two hours, the solvents were evaporated in a current of air, and the residue, which was usually crystalline, was treated with water, filtered, washed well with water, and dried. The products so obtained were entirely satisfactory for the rearrangement reaction.

*Beckmann rearrangement of the oximes.*—The mixture of the dry oximes was suspended in 25 cc. of anhydrous, thiophene-free benzene and treated portionwise with excess of powdered phosphorus pentachloride, usually 3 g. After two to three hours water was added, and the mixture was allowed to stand for three hours more. The solvent was then evaporated in a current of air, and the mixture of amides was collected by filtration, washed with water, and dried.

*Hydrolysis of the substituted amides.*—The general procedure for hydrolysis consisted in refluxing the mixture of amides with 100 cc. of a 25% solution of potassium hydroxide in pure methanol, the condenser being provided with a drying tube containing calcium chloride. A 1-liter round-bottomed flask fitted to a condenser by a ground-glass connection was used. When the hydrolysis was complete, the methanol was distilled from the mixture. Distilled water and benzene were added to the residue in the flask, and the mixture was warmed until two clear layers resulted. After separation of the two solutions, the aqueous solution was extracted three times with benzene in order to remove the amine. Acidification of the filtered aqueous solution yielded the mixture of acids, which were isolated by filtration and/or extraction by benzene. The benzene extract of the amines was shaken with several por-

tions of dilute hydrochloric acid in order to extract the amines, and the benzene solution was evaporated in order to determine if any non-saponifiable material was present.

The mixtures of acids which were obtained were analyzed by the methods worked out in the study of the pinacol-pinacolone rearrangement.<sup>7</sup> Thus, digestion with hot water served to separate benzoic acid (soluble) from *p*-phenylbenzoic acid (insoluble), *m*-toluic acid from *p*-phenylbenzoic acid, *o*-toluic acid from *p*-phenylbenzoic acid, *p*-toluic acid from *p*-phenylbenzoic acid, and benzoic acid from *p*-chlorobenzoic acid. The proportion of *p*-anisic acid in the mixture of this acid and benzoic acid was determined by means of a methoxyl determination, performed according to the method of Vieböck and Schwappach<sup>8</sup>. The mixtures of benzoic acid and the toluic acids were analyzed by oxidizing the toluic acids to the corresponding phthalic acids, which could be separated readily from the soluble benzoic acid. As a rule synthetic mixtures of the acids were analyzed at the same time for comparison.

*Isolation of the two stereoisomeric phenyl p-biphenyl ketoximes.*—Fifteen grams of phenyl *p*-biphenyl ketone was oximated, and the mixture of oximes was recrystallized from methanol. The first crop of crystals consisted principally of fine, gleaming needles of the *anti*-phenyl *p*-biphenyl ketoxime, which is less soluble than its stereoisomer. By further recrystallization this oxime was obtained perfectly pure; m. p. 200°. The filtrate from which this oxime had been separated was concentrated and allowed to stand for several days so that some evaporation took place. Under these conditions the solution deposited the *syn*-phenyl *p*-biphenyl ketoxime as stout, monoclinic prisms along with fine needles of the isomer and a fine mixture of both forms. The large prisms were separated from the mixture mechanically and purified by recrystallization from methanol; m.p. 173°.

*Rearrangement of anti-phenyl p-biphenyl ketoxime.*—Rearrangement of the oxime in the usual manner by means of phosphorus pentachloride in anhydrous benzene yielded an anilide, which on hydrolysis gave a quantitative yield of *p*-phenylbenzoic acid and aniline; no *p*-aminobiphenyl or benzoic acid could be detected.

*Conversion of anti-phenyl p-biphenyl ketoxime to the equilibrium mixture of the oximes.*—A 1.0-g. portion of the oxime, 0.4 g. of hydroxylamine hydrochloride, 2 cc. of absolute alcohol, 2 cc. of pyridine and 2 drops of water were heated on a steam bath for two hours. Rearrangement of the product which was isolated from the solution, followed by hydrolysis of the rearrangement product yielded 53.5% of *p*-phenylbenzoic acid and 44% of *p*-aminobiphenyl.

*Rearrangement of syn-phenyl p-biphenyl ketoxime.*—Rearrangement of a sample of this oxime in the usual manner gave only *N*-(*p*-biphenyl)benzamide, for hydrolysis of the amide yielded benzoic acid and *p*-aminobiphenyl; no trace of *p*-phenylbenzoic acid was found.

*Conversion of syn-phenyl p-biphenyl ketoxime to the equilibrium mixture of the oximes.*—A sample of this oxime treated in the manner described for the *anti* isomer gave a mixture of oximes, which on rearrangement, followed by hydrolysis of the amides, yielded 54% of *p*-phenylbenzoic acid and 46% of benzoic acid.

*Rearrangement of the phenyl p-biphenyl ketoximes prepared by Koller's method.*—Koller oximated phenyl *p*-biphenyl ketone in an alkaline aqueous-alcoholic solution.

<sup>7</sup> BACHMANN AND MOSER, *J. Am. Chem. Soc.*, **54**, 1124 (1932); BACHMANN, *ibid.*, **54**, 2112 (1932); BACHMANN AND STERNBERGER, **56**, 170 (1934); BACHMANN AND FERGUSON, *ibid.*, **56**, 2081 (1934).

<sup>8</sup> VIEBÖCK AND SCHWAPPACH, *Ber.*, **63**, 2818 (1930).



Since he was able to isolate only one oxime from his product, we have repeated his procedure. To a solution of 1.26 g. of the ketone in 25 cc. of alcohol was added an aqueous solution of 0.84 g. of hydroxylamine hydrochloride and 2.1 g. of potassium hydroxide. In order to dissolve all of the ketone, 11 cc. of alcohol was added and the mixture was refluxed for sixteen hours. The mixture of oximes was isolated and rearranged, and the products of the rearrangement were hydrolyzed; in this manner a mixture of *p*-phenylbenzoic acid (48%) and benzoic acid (39%) was obtained, an indication that both oximes were present in the product of oximation.

*Rearrangement by other reagents.*—Ten cc. of concentrated sulfuric acid was added to 50 cc. of glacial acetic acid containing the mixture of oximes obtained from 0.005 gram mole of phenyl *p*-biphenyl ketone. The solution was heated for twenty minutes on a steam bath and then kept at the boiling point for fifteen minutes. In one run, 1.19 g. (90%) of the theoretical weight of the substituted amides was obtained. Hydrolysis of the mixture of amides yielded 53% of *p*-phenylbenzoic acid (in addition to benzoic acid), in good agreement with the experiments in which phosphorus pentachloride was employed. In a number of runs the yields of products were rather low.

Rearrangement of the phenyl *p*-biphenyl ketoximes by phosphorus trichloride in anhydrous benzene was incomplete even after twenty-four hours at room temperature. The reagent was also tried on benzophenone oxime. Two g. of phosphorus trichloride was added to a mixture of 2 g. of benzophenone oxime and 25 cc. of benzene. After three days at room temperature, the benzene was evaporated and the solid was collected by filtration, washed with water and dried. After digestion with hot 60–70° petroleum ether, 0.87 g. (44%) of benzanilide remained. From the petroleum ether extract was isolated 1.0 g. of benzophenone.

*Methyl p-biphenyl ketoximes.*—By hydrolysis of the products obtained by rearrangement of the oxime mixture from 0.01 gram mole of methyl *p*-biphenyl ketone, 0.04 g. (1%) of *p*-phenylbenzoic acid was obtained. In addition 3.23 g. (95.6%) of *p*-aminobiphenyl was isolated, thus accounting for 96.6% of the products.

Ingersoll and White<sup>9</sup> obtained an 80–82% yield of the *anti-p*-biphenyl methyl ketoxime in the form of yellow plates melting at 186° by oximation of methyl *p*-biphenyl ketone with hydroxylamine hydrochloride and 30% sodium hydroxide. We isolated this oxime in nearly quantitative yield by the pyridine method, and by recrystallization from alcohol obtained it as colorless needles which melted at 186–187°.

*Phenyl o-tolyl ketoximes.*—Forty hours of heating was found to be necessary to oximate phenyl *o*-tolyl ketone completely. Rearrangement of the mixture of oximes gave a 98% yield of the substituted amides. The proportion of *o*-toluic acid in the mixture of benzoic acid and *o*-toluic acid obtained by hydrolysis of the amides was determined by oxidizing the *o*-toluic acid to phthalic acid by alkaline permanganate solution, and separating the benzoic acid and phthalic acid by means of hot carbon tetrachloride, in which the phthalic acid is nearly insoluble.

*o-Tolyl p-biphenyl ketoximes.*—Even forty-eight hours of heating proved to be insufficient for complete oximation of *o*-tolyl *p*-biphenyl ketone. In the best runs only a 75% yield of acids was obtained in the final step. The mixture of *o*-toluic acid and *p*-phenylbenzoic acid was readily separated by digestion with hot water, which dissolved the former but not the latter.

*Methyl 1-anthryl ketoximes.*—1-Acetylanthracene was prepared according to the method of the German patent 492,247; our product melted at 106.5–108° instead of

<sup>9</sup> INGERSOLL AND WHITE, *J. Am. Chem. Soc.*, **54**, 274 (1932).

the reported 103–105°. During the oximation process, the solution turned dark-green, and the oil remaining after evaporation of the solvent retained the dark color. After the customary treatment with water, the oximes crystallized. During the rearrangement with phosphorus pentachloride the mixture became very dark and the products refused to crystallize. By hydrolysis a 20% yield of 1-aminoanthracene (m.p. 118–119°) and a small amount of 1-anthroic acid were isolated. Since quantitative yields of the products could not be obtained the work on this ketone was abandoned. 9-Acetylanthracene, likewise, gave unsatisfactory results.

*9-Benzoylanthracene*.—This ketone was prepared by the Perrier modification of the Friedel-Crafts reaction. A mixture of 3.5 g. of aluminum chloride and 3.5 g. of benzoyl chloride was warmed gently over a free flame until a clear solution resulted. The cooled product was dissolved in 20 cc. of warm carbon disulfide, and to the cooled solution was added 4.5 g. of anthracene. The red-black precipitate which formed slowly during the course of one-half hour of cooling by ice and water was filtered, dried and hydrolyzed by dilute hydrochloric acid. The ketone which resulted was recrystallized from alcohol in order to free it from anthracene. Sublimation and recrystallization from ethyl acetate gave bright-yellow, diamond-shaped crystals of 9-benzoylanthracene; m.p. 145.5–146°; yield, 85%. Heating a mixture of 0.564 g. of the ketone, 0.2 g. of hydroxylamine hydrochloride, 1.5 cc. of pyridine and 1.5 cc. of absolute alcohol for two hours, for twenty-four hours, and even for three weeks failed to give any of the oxime.

*Phenyl 2-fluoryl ketoximes*.—Phenyl 2-fluoryl ketone (2-benzoylfluorene) was prepared by adding 16.6 g. of anthracene to a solution of the complex from 14 g. of benzoyl chloride and 14 g. of aluminum chloride in 80 cc. of carbon disulfide. The bright-yellow solid which resulted was filtered off and washed with carbon disulfide in order to free it from a red by-product. The precipitate was hydrolyzed with dilute hydrochloric acid and the colorless ketone, after being freed from traces of carbon disulfide, was recrystallized from alcohol (450 cc.); m.p. 124–124.7°; yield, 24 g. (89%). By sublimation at 0.4 mm. the ketone was obtained as colorless, glistening needles which melted at 124.5–125°. Ray and Levine,<sup>10</sup> using the Perrier method (no details given), reported a 61% yield of ketone melting at 122°.

When 2.7 g. of the ketone was oximated, precipitation of the oximes started after about twenty minutes of heating. The mixture of substituted amides obtained by rearrangement of the oximes proved to be very resistant to hydrolysis by potassium hydroxide in methanol. The amide, which was particularly difficult to hydrolyze, was found to be *N*-phenyl-2-fluorencarboxylic acid amide (m. p. 255–256°); this compound could be readily isolated after partial hydrolysis had been effected, and its structure was established by synthesis. The isomeric amide, *N*-(2-fluoryl-benzamide (m.p. of a synthetic sample, 215°) was more readily hydrolyzed.

Complete hydrolysis of the mixture of amides was finally accomplished by refluxing them for four weeks with a 5% solution of hydrochloric acid in ethanol. After removal of the amine hydrochlorides (from which a 46% yield of 2-aminofluorene was isolated), the residue was heated with potassium hydroxide in order to hydrolyze any esters that had been formed. The mixture of acids which was isolated consisted of 54% (by moles) of 2-fluorencarboxylic acid and 46% of benzoic acid. The two acids were separated by digestion with hot water, which dissolved the benzoic acid.

<sup>10</sup> RAY AND LEVINE, J. ORG. CHEM., **2**, 267 (1937).



## SUMMARY

Pure *syn*- and *anti*-phenyl *p*-biphenyl ketoximes have been isolated from the mixture of the two oximes produced on oximation of phenyl *p*-biphenyl ketone.

Under the conditions employed for making the oximes from the ketone, each of the stereoisomeric phenyl *p*-biphenyl ketoximes is converted to the same mixture of the two oximes that is formed on oximation of the ketone.

The relative proportions of the *syn* and *anti* oximes produced on oximation were determined for thirteen ketones.

The existence of a number of new oximes has been established by means of the quantitative methods employed in the investigation.

Twelve new substituted amides have been synthesized.









